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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,645	02/25/2002	Hiroyuki Miyachi	219214US0PCT	6387

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EXAMINER

ANDERSON, REBECCA L

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 05/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/049,645

Applicant(s)

MIYACHI ET AL.

Examiner

Rebecca L. Anderson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 13-21 and 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 5, 6, 9, 22 and 24 is/are rejected.
- 7) ☒ Claim(s) 3, 4, 7 and 8 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### **DETAILED ACTION**

Claims 1-9 and 13-24 are currently pending in the instant application. Claims 1, 2, 5, 6, 9, 22 and 24 are rejected, claims 3, 4, 7 and 8 are objected and claims 13-21 and 23 are withdrawn from further consideration.

### ***Election/Restrictions***

Newly submitted claims 13-21 and 23 directed to inventions that are independent or distinct from the invention originally claimed for the following reasons: Claims 13-21 are drawn to methods of use for the benzylthiazolidine-2,4-dione compounds as found in claim 1 and claim 23 is drawn to the process for the preparation of products of the compounds as found in claim 1. The current invention of claims 1-9, 22 and 24, product claims, are related to the claims 13-21 as product and process of using. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the process for using the product as claimed can be practiced with another materially different product such as the compounds found in US Patent No. 5,061,717 which are blood glucose lowering agents. The current invention of claims 1-9, 22 and 24, product claims, are related to the claim 23 as product and process of making. The inventions can be shown to be distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP §

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806.05(f)). In the instant case the process as claimed can be used to make other and materially different products such as those products as found in U.S. 5,061,717.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 13-21 and 23 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

### ***Response to Amendment and Arguments***

Applicants amendment filed 28 February 2003 has been considered and entered as Paper No. 7. Applicants cancellation of claims 10-12 has overcome the objection and rejection under 35 U.S.C. 112 to these claims. Applicants amendment to claim 1 has overcome the 35 U.S.C. 112 rejection of claim 1. Applicant's arguments with respect to the rejection of claims 1, 2, 5, 6, and 9-12 under 35 U.S.C. 103(a) have been considered but are moot in view of the new ground(s) of rejection. In addition to applicants arguments and amendments, applicant has also provided a comparative data study, Exhibit A, which is a set of experiments comparing the efficacy of the compounds 17, 22, 23 and 28 disclosed by EP'693 with compounds 6, 11, 15, and 22. It is noted that this set of comparative data would be considered an effective showing of unobvious results and would overcome the new 35 U.S.C 103(a) rejection if presented in correct declaration form under 37 C.F.R. 1.132.

***Specification***

The amendment filed 28 February 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: a suitable carrier claimed in claims 22 and 24 is not supported by the original disclosure.

Applicant is required to cancel the new matter in the reply to this Office Action.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly added claims 22 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 22 and 24 are composition claims that contain the phrase "a suitable carrier." However, this subject matter was not described in the specification in any way. The only description found in the specification that closely relates to the a suitable carrier was the description on page 26 and 27 which relates to the administration of the compounds of the invention, however this description is silent to the possible suitable carriers. It is suggested that

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these claims be cancelled to overcome this rejection and the objection to the amendment above.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

Claims 1, 2, 5, 6, 9, 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 846 693 in view of US Patent No. 5,223,522 or in view of WO 97/32863.

The claims at issue teach the benzylthiazolidine-2,4-dione products of the formula (1) wherein B denotes a lower alkyl, lower alkoxy, halogen, trifluoromethyl, trifluoromethoxy, phenyl, phenoxy, or benzyloxy and A denotes -CH<sub>2</sub>CONH-, -NHCONH-, -CH<sub>2</sub>CH<sub>2</sub>CO- or NHCOCH<sub>2</sub>-. These products are useful for the treatment of diabetes, hyperlipidemia and as glucose lowering drugs.

**Determining the scope and contents of the prior art.**

EP 0 846 693 discloses benzyldioxothiazolidylbenzamide compounds of the formula (I) which are useful for the treatment of diabetes and hyperlipidemia (page 2, lines 1-6). The compound of formula (I) is substituted by R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub>. R<sub>1</sub> and R<sub>2</sub>

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can be hydrogen, lower alkyl, lower alkoxy, lower haloalkyl, etc., while R3 can be lower alkoxy, hydroxyl or halogen atom. The dotted line indicated a double or a single bond (page 2 lines 30-46). Furthermore, EP 0 846 693 discloses specific compounds wherein the dotted line is a single bond, and R3 is **methoxy** (compound examples 17 where R1 is 3-CF3, 19 where R1 is 2-CF3, 22 where R1 is 4-t-Bu and 26 where R1 is 4-MeO in Table 5, pages 12-13).

US Patent No. 5,223,522 discloses thiazolidinedione compounds of the formula (I) wherein X1 and X2 can be H, methyl, CG3, phenyl (preferably X2 is hydrogen and X1 is 4-phenyl, 4-benzyloxy, hydrogen, or 2-methoxy). R is hydrogen or methyl, preferably hydrogen. n is 0 to 1, preferably 0. A and B are CH, X is S, SO, SO2, CH2, CHOH, CO (preferably CO), Y is CHR1 or NR2, and Z is CHR3, or preferably **CH2CH2** (column 4 lines 1-40). These compounds are blood glucose lowering drugs (column 4, line 65).

WO 97/32863 discloses thiazolidine-2,4-dione derivative compounds useful for treatment of diabetes (abstract) wherein in the compound of formula (I-a), A can be **CONH** or **NHCO** (page 4). Furthermore, WO 97/32863 discloses specific examples 3-24 on page 29 where A is **CONH** and R1 is substituted and unsubstituted phenyl.

**Ascertaining the differences between the prior art and the claims at issue.**

The difference between the prior art of EO 0 846 693 and the claims at issue is that the prior art compound has CH2NHCO in the position equivalent to substituent A on the applicants claimed formula (1).

The differences between the prior art of US Patent No. 5223522 and the claims at issue is that the prior art compounds do not have a methoxy substituent on the benzylthiazolidine-2, 4-dione and are positional isomers of the compounds as instantly claimed.

The difference between the prior art of WO 97/32863 and the claims at issue is that the prior art compounds do not have a methoxy substituent on the benzylthiazolidine-2, 4-dione and are positional isomers of the compounds as instantly claimed.

**Resolving the level of ordinary skill in the pertinent art.**

However, minus the showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention when faced with EP 0 846 693 and either US Patent No. 5223522 or WO 97/32863 to create products which are useful for the treatment of diabetes and as glucose lowering drugs, wherein A is CH<sub>2</sub>CH<sub>2</sub>CO or CH<sub>2</sub>CONH and the benzylthiazolidine-2, 4-dione is substituted by methoxy, due to the similar chemical structure (benzylthiazolidine-2, 4-dione) of the compounds of the prior art, which is seen in the disclosure of WO 97/32863 that discloses CH<sub>2</sub>NHCO (the substituent found on the compounds from EP 0 846 693) is a possible substituent on the compounds useful as blood glucose lowering drugs along with CH<sub>2</sub>CONH, which is the substituent A as instantly claimed. The reasoning behind the finding of obviousness is that WO 97/32863 discloses the interchangeability of the aminocarbonyl groups CH<sub>2</sub>NHCO and CH<sub>2</sub>CONH in compounds which are useful for the treatment of diabetes and therefore one would be motivated to prepare compounds as found in EP 0 846 693,



which are substituted with methoxy, with the aminocarbonyl group  $\text{CH}_2\text{CONH}$  in the position of  $\text{CH}_2\text{NHCO}$  when faced with WO 97/32863 which would be useful benzylthiazolidine-2,4-dione compounds as blood glucose lowering drugs. The same reasoning applies to EP 0 846 693 and U.S. Patent No. 5,223,522. It would have been obvious to one of ordinary skill in the art at the time of the invention to create products which are useful for blood glucose lowering, wherein A is  $\text{CH}_2\text{CONH}$  and the benzylthiazolidine-2, 4-dione is substituted by methoxy due to the similar chemical structure (benzylthiazolidine-2, 4-dione) of the compounds of the prior art, which is seen in the disclosure of U.S. Patent No. 5,223,522 that discloses the interchangeability of  $\text{CH}_2\text{CH}_2\text{CO}$  and  $\text{CH}_2\text{NHCO}$  in compounds which are usefule for blood glucose lowering agents, ( $\text{CH}_2\text{CH}_2\text{CO}$  is discloses as the preference for X and Z and it is also disclosed that Z can be  $\text{CHR}_3$ , Y can be  $\text{NR}_2$  and X is preferable CO (the substituent A as found on the compounds from EP 0 846 693)). The reasoning behind the finding of boviousness is that U.S. Patent No. 5,223,522 discloses the interchangeability of  $\text{CH}_2\text{CH}_2\text{CO}$  and  $\text{CH}_2\text{NHCO}$  in compounds which are useful as blood glucose lowering agents and therefore one would be motivated to prepare compounds as found in EP 0 846 693, which are substituted with methoxy, with the group  $\text{CH}_2\text{CH}_2\text{CO}$  in the position of  $\text{CH}_2\text{NHCO}$  when faced with U.S. Patent No. 5,223,522 which would be useful benzylthiazolidine-2,4-dione compounds as blood glucose lowering agents. Again, the motivation for combining these references is the creation of other useful benzylthiazolidine-2, 4-dione compounds useful for the treatment of diabetes and hyperlipidemia.

### ***Claim Objections***

Claims 3 and 4 are objected to as being dependent upon a rejected base claim, but would appear allowable over the prior art of record if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 7 and 8 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claims 7 and 8 claim compounds as found in claim 1 wherein one of the compounds is [ a specific compound name]. However, this does not further limit the previous claim as the specifically named compound is included in claim 1. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. It is suggested that these claims be amended to read --The compound according to claim 1 which is [specific compound name]--.

### **Conclusion**

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (703) 605-1157. Mrs. Anderson can normally be reached Monday through Friday 7:00AM to 3:30PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph McKane, can be reached at (703) 308-4537.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone numbers are (703) 308-1235 and (703) 308-0196.

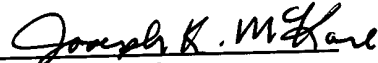
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A facsimile center has been established. The hours of operation are Monday through Friday, 8:45AM to 4:45PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4242, (703) 305-3592, and (703) 305-3014.



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